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EXAMINER

SPIEGLER, ALEXANDER H

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 11 27 2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/817,014

Applicant(s)

REMACLE ET AL.

Examiner

Alexander H. Spiegler

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 C.F.R. 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 C.F.R. 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 09 September 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-39 is/are pending in the application.
- 4a) Of the above claim(s) 24-37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-23, 38 and 39 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 11.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election without traverse of Group I (claims 1-23 and 38-39) in Paper No. 13, filed on September 9<sup>th</sup>, 2002 is acknowledged.

### ***Specification***

2. A substitute specification excluding the claims is required pursuant to 37 CFR 1.125(a) because the number and nature of the amendments of the application papers renders it difficult to consider the application.

A substitute specification filed under 37 CFR 1.125(a) must only contain subject matter from the original specification and any previously entered amendment under 37 CFR 1.121. If the substitute specification contains additional subject matter not of record, the substitute specification must be filed under 37 CFR 1.125(b) and must be accompanied by: 1) a statement that the substitute specification contains no new matter; and 2) a marked-up copy showing the amendments to be made via the substitute specification relative to the specification at the time the substitute specification is filed.

3. Claims 11-13 recite, "characterized in that" which appears to be superfluous, and could be deleted from the claims.

### ***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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5. Claims 1-23 and 38-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-23 and 38-39 over "by a detecting" because it is not as to what a "detecting" is.

B) Claims 1-23 and 38-39 over "original" nucleotide sequences because it is not clear as to what an "original" nucleotide sequence is, and furthermore, it is not defined in the specification.

C) Claims 1-23 and 38-39 over "a unique set of primers" because it is not clear as to what constitutes a "unique" set of primers.

D) Claims 1-23 and 38-39 over "at least part of original nucleotide sequences into target" because it is not clear as to how one amplifies "part of original nucleotide sequences *into*" target nucleotide sequences to be detected.

E) Claims 1-23 and 38-39 over "preferably" because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

F) Claims 1-23 and 38-39 over "specific of an organism" because this wording is vague and confusing.

G) Claims 1-23 and 38-39 over "forms results in said signal at the expected locations" because it is not clear what are considered to be "results", and "the expected locations" lacks antecedent basis.

H) Claims 1-23 and 38-39, because the claims do not recite a final process step which clearly relates back to the preamble.

I) Claims 2 and 4 over "the amplified homologous original nucleotide sequence" because this recitation lacks antecedent basis.

J) Claims 3-5 over "the same primer pair" because this lacks antecedent basis.

K) Claim 4 over "mRNA first retrotranscribed into cDNA" because it is not clear as to what "*retrotranscribed*" means.

L) Claim 5 over "the copy of the homologous original nucleotide sequences" lacks antecedent basis.

M) Claim 6 over "the same capture nucleotides sequences specific for one organism" lacks antecedent basis.

N) Claims 7-8 over "the specific sequence of the capture sequence" lacks antecedent basis. Furthermore, claim 7 is indefinite over "able to hybridize with their corresponding target nucleotide sequence, is separate from the surface of the solid support by a spacer" because this is vague and confusing, and it is not clear as to what the "spacer" is.

O) Claim 9 over "superior to 10 fmoles" because it is not clear as to what constitutes "superior" to 10 fmoles.

P) Claim 10 over "presents an homology" because it is not clear how a sequence "presents an homology".

Q) Regarding claim 12, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

R) Claim 13 over "mixture thereof" because it is not clear as what kind of a mixture can be made with the elements of the claim.

S) Claim 14 over "submitted to a retro-transcription" because it is not clear who RNA is "submitted to a retro-transcription". Also, "the 3' or 5' end" lacks antecedent basis, "possibly" because it is not clear whether or not this "stopper sequence" is necessary, and furthermore, it is not clear what a "stopper sequence" is.

T) Claim 15 is indefinite due to the improper expression of alternative limitations. "Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being 'selected from the group consisting of A, B, and C'." (MPEP 2173.05(d)). To overcome this rejection, the claim may be amended to recite "and" where it now recites "and/or". Furthermore, it is not clear as to what *FemA* "genetic sequences" are.

U) Claim 16 over "capture nucleotide sequences specific of the homologous sequences specific for the binding with the homologous target nucleotide sequence together with a consensus sequence or a common detection" because this phrase is vague and confusing, and it is not clear as to what these capture nucleotide sequences are.

V) Claims 18-23 over "the original sequence" because this recitation lacks antecedent basis. Additionally, it is not clear as to what members belong to the MAGE, HLA-A, protein G, gene family or cytochrome P450 forms family. The specification does not describe or define the these families.

#### ***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-14, 18-23 and 38-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Brown et al. (USPN 5,807,522).

Due to the lack of clarity of the claims, the claims have been interpreted as drawn to methods of identifying and/or quantifying an organism or part of an organism by hybridizing labeled target sequences to capture nucleotide sequences on an array, wherein the array has a density of at least 4 different bound single stranded capture nucleotide sequences/cm<sup>2</sup>.

Brown teaches:

*"In another aspect, the invention includes a substrate with a surface having a microarray of at least 10<sup>3</sup> distinct polynucleotide or polypeptide biopolymers in a surface area of less than about 1 cm<sup>2</sup>. Each distinct biopolymer (i) is disposed at a separate, defined position in said array, (ii) has a length of at least 50 subunits, and (iii) is present in a defined amount between about 0.1 femtomoles and 100 nanomoles.*

In one embodiment, *the surface is glass slide surface coated with a polycationic polymer, such as polylysine, and the biopolymers are polynucleotides.* In another embodiment, the substrate has a water-impermeable backing, a water-permeable film formed on the backing, and a grid formed on the film. The grid is composed of intersecting water-impervious grid elements extending from said backing to positions raised above the surface of said film, and partitions the film into a plurality of water-impervious cells. *A biopolymer array is formed within each well.*

More generally, there is provided *a substrate for use in detecting binding of labeled polynucleotides to one or more of a plurality different-sequence, immobilized polynucleotides.* The substrate includes, in one aspect, a glass support, a coating of a polycationic polymer, such as polylysine, on said surface of the support, and an array of distinct polynucleotides electrostatically bound non-covalently to said coating, where each distinct biopolymer is disposed at a separate, defined position in a surface array of polynucleotides.

Also forming part of the invention is *a method of detecting differential expression of each of a plurality of genes in a first cell type, with respect to expression of the same genes in a second cell type. In practicing the method, there is first produced fluorescent-labeled cDNAs from mRNAs isolated from the two cells types, where the cDNAs from the first and second cell types are labeled with first and second different fluorescent reporters.*

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*A mixture of the labeled cDNAs from the two cell types is added to an array of polynucleotides representing a plurality of known genes derived from the two cell types, under conditions that result in hybridization of the cDNAs to complementary-sequence polynucleotides in the array. The array is then examined by fluorescence under fluorescence excitation conditions in which (i) polynucleotides in the array that are hybridized predominantly to cDNAs derived from one of the first or second cell types give a distinct first or second fluorescence emission color, respectively, and (ii) polynucleotides in the array that are hybridized to substantially equal numbers of cDNAs derived from the first and second cell types give a distinct combined fluorescence emission color, respectively. The relative expression of known genes in the two cell types can then be determined by the observed fluorescence emission color of each spot.” (col. 4)*

Additionally, Brown teaches a plurality of uses for the microarray described above, such as “large scale hybridization assays in numerous genetic applications, including genetic and physical mapping of genomes, monitoring of gene expression, DNA sequencing, genetic diagnosis, genotyping of organisms, etc.” (col. 14-15, see also Example 3). Brown also teaches the target nucleotide sequence can amplified prior to being hybridized to the capture nucleotide sequences on an array (col. 15), and that the target can be a microorganism (Example 1).

Claims 18-23 are rejected herein because of the indefiniteness of the claims.

8. Claims 1-14, 18-23 and 38-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Fodor et al. (USPN 5,80,992).

Due to the lack of clarity of the claims, the claims have been interpreted as drawn to methods of identifying and/or quantifying an organism or part of an organism by hybridizing labeled target sequences to capture nucleotide sequences on an array, wherein the array has a density of at least 4 different bound single stranded capture nucleotide sequences/cm<sup>2</sup>.

Fodor teaches:

*“The present invention provides a composition comprising a plurality of positionally distinguishable sequence specific reagents attached to a solid substrate, which reagents are capable of specifically binding to a predetermined subunit sequence of a preselected multi-subunit length having at least three subunits, said reagents representing substantially all*



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*possible sequences of said preselected length. In some embodiments, the subunit sequence is a polynucleotide or a polypeptide, in others the preselected multi-subunit length is five subunits and the subunit sequence is a polynucleotide sequence. In other embodiments, the specific reagent is an oligonucleotide of at least about five nucleotides. Alternatively, the specific reagent is a monoclonal antibody. Usually the specific reagents are all attached to a single solid substrate, and the reagents comprise about 3000 different sequences. In other embodiments, the reagents represents at least about 25% of the possible subsequences of said preselected length. Usually, the reagents are localized in regions of the substrate having a density of at least 25 regions per square centimeter, and often the substrate has a surface area of less than about 4 square centimeters.*

The present invention also provides methods for analyzing a sequence of a polynucleotide or a polypeptide, said method comprising the step of: a) exposing said polynucleotide or polypeptide to a composition as described.” (col. 2-3).

Fodor also teaches the target nucleotide sequence can be labeled (col. 4), a plurality of uses for the composition detailed above, such as sequencing, mapping, screening procedures, etc. (col. 9, 11, 19-36, 48-55, and 57-61). Claims 18-23 are rejected herein because of the indefiniteness of the claims.

### ***Claim Rejections - 35 USC § 103***

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 15-17 rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (USPN 5,807,522) or Fodor et al. (USPN 5,800,992), as applied to claims 1-14, 18-23 and 38-39 above, and further in view of Vannuffel et al. (WO 99/16780, cited in the IDS).

The teachings of Brown and Fodor are presented above. Specifically, Brown and Fodor

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each teaches methods of identifying and/or quantifying an organism or part of an organism by hybridizing labeled target sequences to capture nucleotide sequences on an array, wherein the array has a density of at least 4 different bound single stranded capture nucleotide sequences/cm<sup>2</sup>. Brown and Fodor do not teach the specific detection of Staphylococci species using consensus sequences from the *femA* nucleotide sequence.

However, Vannuffel teaches the specific detection of Staphylococci species using consensus sequences from the *femA* nucleotide sequence (see abstract). Vannuffel teaches the use of specific primers and probes of the consensus *femA* sequence (pgs. 4, 7 and 8-10). More specifically, Vannuffel teaches a method for identification and/or quantification of staphylococcal species comprising, obtaining a staphylococcal species from a biological sample, possibly purifying and amplifying said sample, and then identifying said species through hybridization on an oligonucleotide array, wherein the consensus sequences of *femA* are used as capture nucleotide sequences (pgs. 11-12). Vannuffel also teaches that the method can be advantageously combined with another specific detection step of possible resistance to antibiotics. Examples 1-7 of Vannuffel further exemplify additional embodiments of the methods outlined above.

In view of the teachings of Vannuffel, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Brown (or Fodor) so as to have included the consensus sequences (i.e. primers and probes) specific for the *femA* sequence of Staphylococcal species, in order to have achieved the benefit of providing an effective means of detecting specific species of the Staphylococci genus for use in diagnosing staphylococcal infections, for example.

***Conclusion***

11. No claims are allowable.
12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

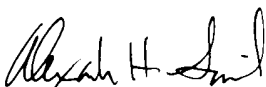
Gentalen et al. (USPN 6,306,643) because this reference essentially teaches the same elements of both Brown et al. (USPN 5,807,522) and Fodor et al. (USPN 5,800,992) detailed above.

***Correspondence***

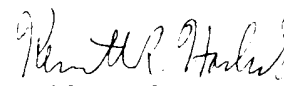
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014. Applicant is also invited to contact the TC 1600 Customer Service Hotline at (703) 308-0198.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Alexander H. Spiegler  
November 25, 2002



KENNETH R. HORLICK, PH.D  
PRIMARY EXAMINER

11/26/02